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Structural and Physico-Chemical Interpretation (SPCI) of QSAR Models and Its Comparison with Matched Molecular Pair Analysis

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Abstract

© 2016 American Chemical Society.This paper describes the Structural and Physico-Chemical Interpretation (SPCI) approach, which is an extension of a recently reported method for interpretation of quantitative structure-activity relationship (QSAR) models. This approach can efficiently be used to reveal structural motifs and the major physicochemical factors affecting the investigated properties. Its efficacy was demonstrated both on the classical Free-Wilson data set and on several data sets with different end points (permeability of the blood-brain barrier, fibrinogen receptor antagonists, acute oral toxicity). Structure-activity patterns extracted from QSAR models with SPCI were in good correspondence with experimentally observed relationships and molecular docking, regardless of the machine learning method used. Comparison of SPCI with the matched molecular pair (MMP) method clearly shows an advantage of our approach over MMP, especially for small or structurally diverse data sets. The developed approach has been implemented in the SPCI software tool with a graphical user interface, which is publicly available at http://qsar4u.com/pages/sirms-qsar.php.

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